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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/568,433

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Gilles Pain

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EXAMINER

JARRELL, NOBLE E

ART UNIT

PAPER NUMBER

1624

MAIL DATE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/568,433	<b>Applicant(s)</b> PAIN ET AL.	
	<b>Examiner</b> NOBLE JARRELL	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8-11, 14-22, 24 and 26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-11, 14-22, 24 and 26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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## **DETAILED ACTION**

### ***Response to Arguments***

1. The objection to the abstract has been overcome by the amendment filed 10 November 2008.
2. The rejections under 35 U.S.C. 2nd paragraph regarding the phrase "e.g." and the omission of essential subject matter have been overcome by the amendment filed 10 November 2008.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-6, 8-11, 14-22, and 24, and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for enantiomer(s), diastereomers(s), or salt(s) of formula I, does not reasonably provide enablement for a hydrate or solvate of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. While applicants are enabled for the preparation of for enantiomer(s), diastereomers(s), or salt(s) of formula I, they do not show solvates or hydrates of formula I can be prepared.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether

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undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to compounds and compositions of formula I, where formula I is composed of a piperazine ring connected to a phenyl ring through an alkyl-C(O) linker. The linker is modified with a C(OR)(C(O)NHOH) group, where variable R is hydrogen, alkyl, or cycloalkyl.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

Vippagunta et al. (*Advanced Drug Delivery Reviews*, **2001**, 48, 3-26) teach that solvate or hydrate formation is unpredictable even within a series of related molecules because each compound responds uniquely to solvate formation (page 18, section 3.4).

*(5) The relative skill of those in the art:*

One of ordinary skill in the art can replicate the preparation of example 62 of the specification (pages 60-67).

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

The specification has provided guidance for preparation of for enantiomer(s), diastereomers(s), or salt(s) of formula I.

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However, the specification does not provide guidance for preparation of a solvate or hydrate of formula I.

*(8) The quantity of experimentation necessary:*

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-6, 8-11, 14-22, and 24, and 26 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims. This rejection is maintained because applicants have not shown that compound of the instant invention can predictably form solvates or hydrates. As previously stated, Vippagunta et al. state that it is unpredictable whether or not a polymorphic form will form because each molecule has a unique chemical nature.

5. Claims 24 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of arthritis or osteoarthritis, does not reasonably provide enablement for prevention of arthritis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

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Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to treatment or prevention of disorder related to inhibition of MMP 9 or 12 with a compound of formula I or a composition comprising the same.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

Clark et al. (*Expert Opinion in Therapeutic Targets*, **2003**, 7(1), 19-34) teach that arthritis is related to inhibition of MMP 9. Roach (*Expert Opinion in Drug Discovery*, **2008**, 3(5), 475-86) teaches that MMP 9 is related to cartilage erosion, and in turn, osteoarthritis.

Both osteoarthritis and arthritis are not preventable with drugs, but by other methods ("Osteoarthritis Prevention - WebMD",

<http://www.webmd.com/osteoarthritis/tc/osteoarthritis-prevention>, accessed May 5, 2008;

"Arthritis Prevention", <http://www.symptomsof arthritis.com/arthritis-Prevention.html>,

accessed May 5, 2008). Since prophylaxis is defined as prevention of a disorder

("Prophylaxis definition",

<http://www.medterms.com/script/main/art.asp?articlekey=12063>, accessed 12

February 2009), this rejection is maintained. Applicants are enabled only for the treatment of arthritis.

*(5) The relative skill of those in the art:*

One of ordinary skill in the art can perform a biological assay as described on pages 70-71 of the specification.

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

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The specification has provided guidance for treatment of arthritis or osteoarthritis.

However, the specification does not provide guidance that every disorders associated with inhibition of MMP 9 or MMP 12 can be treated or prevented with a compound of formula I or a composition comprising the same.

*(8) The quantity of experimentation necessary:*

Considering the state of the art as discussed by the references above, particularly with regards to claims 24 and 26 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-6, 8-11, 14-22, and 24, and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-6, 8-11, 14-22, and 24, and 26 are considered indefinite due to the multiple occurrences of "optionally substituted" chemical moieties such as "optionally substituted aryl". Because claims 2-6, 8-11, 14-22, and 24, and 26 depend on claim 1, they are rendered indefinite as well. The specification gives no guidance to what the intended substituents are. Each occurrence of an "optionally substituted" group in these claims renders the claims indefinite.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/  
Examiner, Art Unit 1624

**/James O. Wilson/  
Supervisory Patent Examiner, Art Unit 1624**